

5

distal UP

mAAK(A(T)(A(T)(A(T))TTTImAAAAm

proxinal UP

FIGURE 2A

-66 -59 UP el enent -38 CCCCTCACAAAATTATTTAAATTTCCTCTCTCACCCCCAATAACTCCTA AATCCCCCAC

+1 CACTCACACCEAACACCECCACCCCCCCTCACCCCCTTCTCTCT

FIGURE 2B

Switchable Promoter: Drug Targeting near Cis Element

Direct targeting

C(TTAAAAATAA)C

(TTGAAAATCAA)CGCT

780BP

MEF

·Overlapping Targeting (test for up or down-stream)

(tttTGTT)CGCAC(TTttttt)

UL9

NFkB (tttttGGG[AtTTT]CCttttt]

(aaaaAATT)GTGAGCGCTCAC(AATTtttt) Lac0

NtBBF1 (tttACT[TTA)tttt]

Figure 3

rrnB P1 promoter UP Sequences

RLG3097 (core) (

GACTGCAGTGGTACCTAGGAGG

RLG3074 (wt)

AG**aaaattattitaaattt**cct

RLG4192

GGAAAATTTTTTTCAAAAGTA

RLG4174

TGAAATTTATTTGCGAAAGGG

Figure 4A

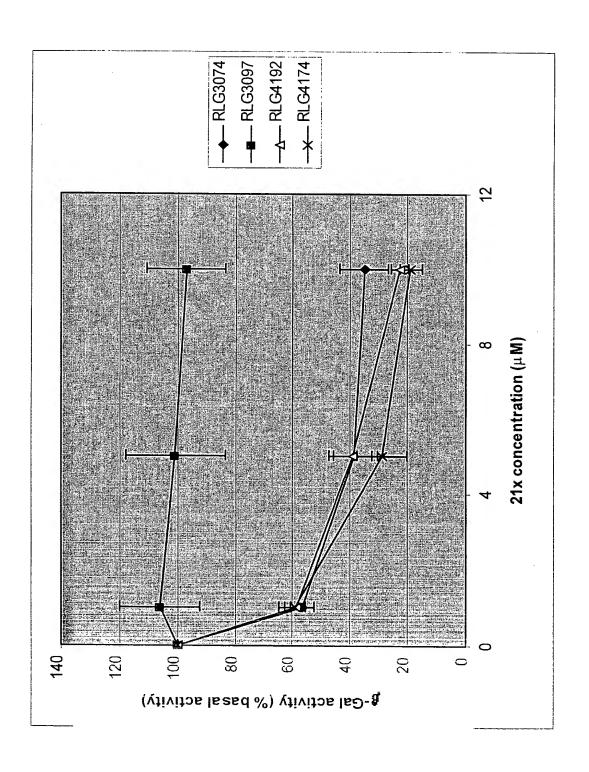


Figure 4B

Figure 5

YK 202RX-B (54-met) 3' GTACCTGC GGTGAC TCGGC ACAAGCGTGAA AAAAACTCCGCTCAGCTACGTGGB 5' YK 202RX-A (54-mer) 5' CATGGACG CCACTG AGCCG TGTTCGCACTT TTTTTGAGGCGAGTGCACC

00 0.0 1 1 1 1 Concentration of 21X (μM)

EIGURE 6

80

09

% signal of no drug control

40

JF 101 (NFKB1) (50mer) (right side)

3, 5' cgac cgtgctcgag TTAACGGGACTTTCCAAaaa cgatcg gact ggactc gctg gcacgagete AATIGCCCTGAAAGGTTttt gctage etga eetgag

JF 102 (NFKB2) (60mer) (right side)

3, 5' cgac cgtgctcgag TTAACGGGAtTTTCCAAaaa cgatcg gact ggactc 3' qctq qcacqaqctc AATTGCCCTAAAAGGTTttt qctaqc ctqa cctqaq gctg gcacgagctc AATTGCCCTaAAAGGTTttt gctagc ctga cctgag

JF 103 (NFKB3) (60mer) (both side)

5' cgac cgtgctcgag aaattGGGAtTTTCCAAaaa cgatcg gact ggactc 3' 3' qctq qcacqaqctc tttaaCCCTaAAAGGTTttt qctaqc ctqa cctqaq 5' gctg gcacgagctc tttaaCCCTaAAAGGTTttt gctagc ctga cctgag

FIGURE 7

120 % signal of no drug control

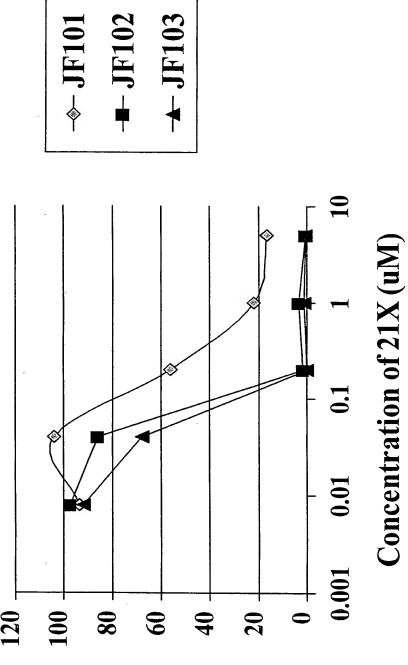


FIGURE 8A

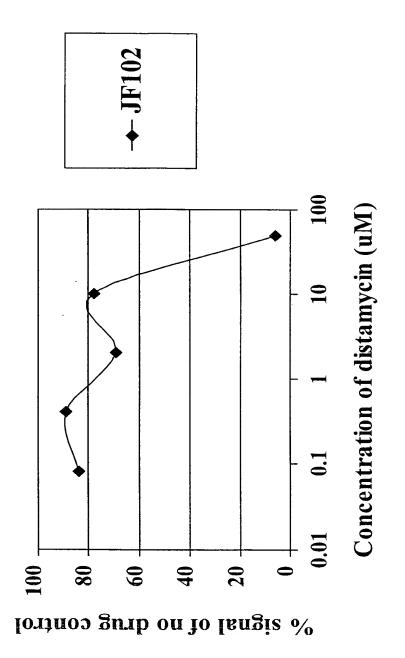
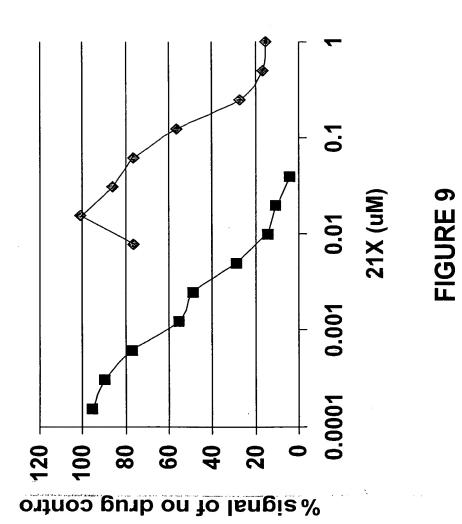


FIGURE 8B



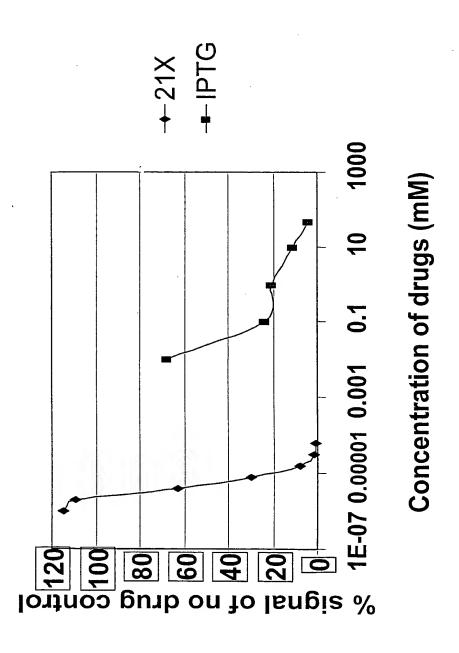


FIGURE 10

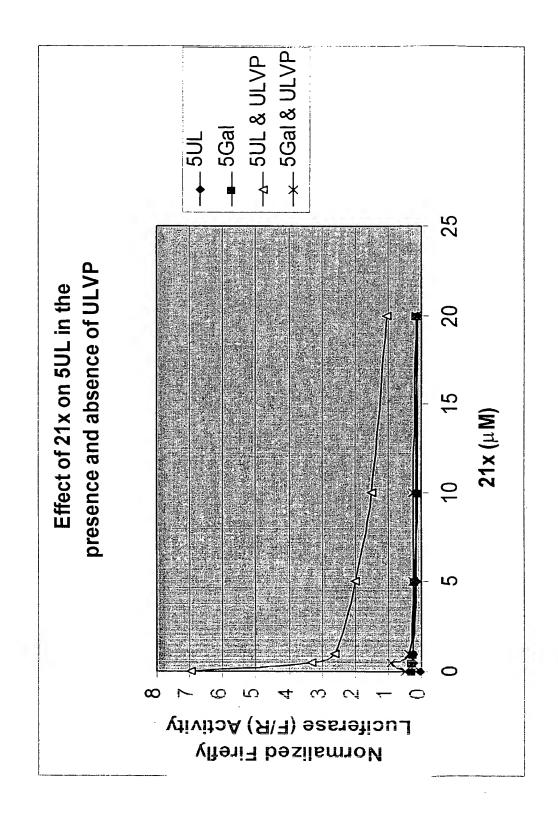
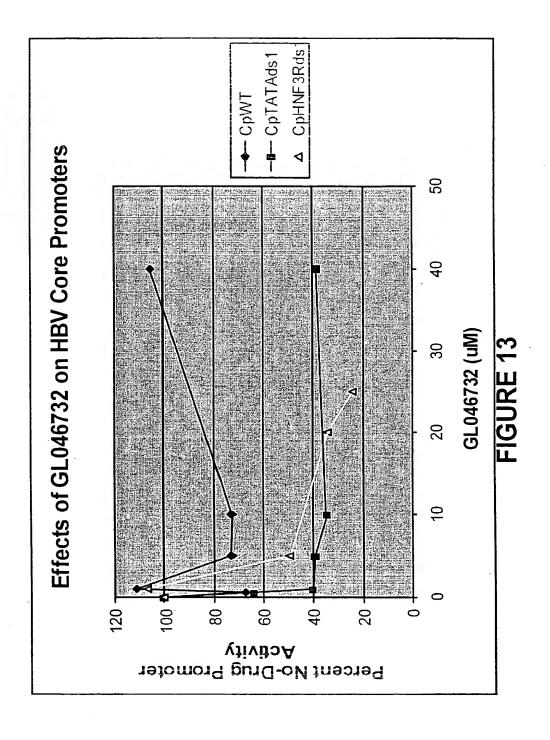


FIGURE 11

10 μM 21 X [μM] 48 hr. M™ 0 H THE PARTY OF THE 140] 120 100 80 8 2 8

Luciferase activity (% wild type activity) n=3

FIGURE 12



TCAATATTGGCCATTAGCCATATTATTCATTGGTTATATAGCATAAATCAATATTGGCTATTGGC CATTGCATACGTTGTATCTATATCATAATATGTACATTTATATTGGCTCATGTCCAATATGACCG CCATGTTGGCATTGATTATTGACTAGTTATTAATAGTAATCAATTACGGGGTCATTAGTTCATAG CCCATATATGGAGTTCCGCGTTACATAACTTACGGTAAATGGCCCGCCTGGCTGACCGCCCAACG ACCCCCGCCCATTGACGTCAATAATGACGTATGTTCCCATAGTAACGCCAATAGGGACTTTCCAT TGACGTCAATGGGTGGAGTATTTACGGTAAACTGCCCACTTGGCAGTACATCAAGTGTATCATAT GCCAAGTCCGCCCCTATTGACGTCAATGACGGTAAATGGCCCGCCTGGCATTATGCCCAGTACA TGACCTTACGGGACTTTCCTACTTGGCAGTACATCTACGTATTAGTCATCGCTATTACCATGGTG ATGCGGTTTTGGCAGTACACCAATGGGCGTGGATAGCGGTTTGACTCACGGGGATTTCCAAGTCT CCACCCCATTGACGTCAATGGGAGTTTGTTTTGGCACCAAAATCAACGGGACTTTCCAAAATGTC GTAACAACTGCGATCGCCCGCCCCGTTGACGCAAATGGGCGGTAGGCGTGTACGGTGGGAGGTCT ATATAAGCAGAGCTCGTTTAGTGAACCGTCAGATCACTAGAAGCTTTATTGCGGTAGTTTATCAC AGTTAAATTGCTAACGCAGTCAGTGCTTCTGACACAACAGTCTCGAACTTAAGCTGCAGTGACTC TCTTAAGGTAGCCTTGCAGAAGTTGGTCGTGAGGCACTGGGCAGGTAAGTATCAAGGTTACAAGA GGCACCTATTGGTCTTACTGACATCCACTTTGCCTTTCTCTCCACAGGTGTCCACTCCCAGTTCA CTCCTGAAAGATGGAGGCGTCGCTGCCGGCCCAGGCCGCGAGACGGAGGAGGTGGGTCTTTTCG TCGAAAAATACCTCCGGTCCGATGTCGCGCCGGCGGAAATTGTCGCGCTCATGCGCAACCTCAAC AGCCTGATGGGACGCACGCGGTTTATTTACCTGGCGTTGCTGGAGGCCTGTCTCCGCGTTCCCAT GGCCACCGCAGCAGCGCCATATTTCGGCGGATCTATGACCACTACGCCACGGGCGTCATCCCCA CGATCAACGTCACCGGAGAGCTGGAGCTCGTGGCCCTGCCCCCACCCTGAACGTAACCCCCGTC TGGGAGCTGTTGTGCCTGTGCAGCACCATGGCCGCGCCCTGCATTGGGACTCGGCGGCCGGGGG ATCTGGGAGGACCTTCGGCCCCGATGACGTGCTGGACCTACTGACCCCCCACTACGACCGCTACA TGCAGCTGGTGTTCGAACTGGGCCACTGTAACGTAACCGACGGACTTCTGCTCTCGGAGGAAGCC GTCAAGCGCGTCGCCGACGCCCTAAGCGGCTGTCCCCCGCGCGGGTCCGTTAGCGAGACGGACCA CGCGGTGGCGCTGTTCAAGATAATCTGGGGCGAACTGTTTGGCGTGCAGATGGCCAAAAGCACGC AGACGTTTCCCGGGGCGGGGGGGTTAAAAACCTCACCAAACAGACAATCGTGGGGTTGTTGGAC GCCCACCACATCGACCACAGCGCCTGCCGGACCCACAGGCAGCTGTACGCCCTGCTTATGGCCCA CAAGCGGGAGTTTGCGGGCGCGCTTCAAGCTACGCGTGCCCGCGTGGGGGCCCTGTTTGCGCA CGCACTCATCCAGCGCCAACCCCAACGCTGACATCATCCTGGAGGCGGCGCTGTCGGAGCTCCCC ACCGAGGCCTGGCCCATGATGCAGGGGGGGGTGAACTTTAGCACCCTAATGAAGCTACTGTCTTC TATCGAACAAGCATGCCCAAAAAAGAAGAAGGTAGATGAATTCCCGGGGATCTCGACGGCCC CCCCGACCGATGTCAGCCTGGGGGACGAGCTCCACTTAGACGGCGAGGACGTGGCGATGGCGCAT GCCGACGCGCTAGACGATTTCGATCTGGACATGTTGGGGGGACGGGGATTCCCCGGGTCCGGGATC GCCAGGGATCCGTCGACTTGACGCGTTGATATCATCTAGAGCGGCCGCAGGTACCTGAATAACTA AGGCCGCTTCCCTTTAGTGAGGGTTAATGCTTCGAGCAGACATGATAAGATACATTGATGAGTTT GGACAAACCACAACTAGAATGCAGTGAAAAAAATGCTTTATTTGTGAAATTTGTGATGCTATTGC TTCAGGTTCAGGGGGAGATGTGGGAGGTTTTTTAAAGCAAGTAAAACCTCTACAAATGTGGTAAA ATCCGATAAGGATCGATTCCGGAGCCTGAATGGCGAATGGACGCGCCCTGTAGCGGCGCATTAAG TTTCGCTTTCTTCCCTTTCTCGCCACGTTCGCCGGCTTTCCCCGTCAAGCTCTAAATCGGG GGCTCCCTTTAGGGTTCCGATTTAGTGCTTTACGGCACCTCGACCCCAAAAAACTTGATTAGGGT GATGGTTCACGTAGTGGGCCATCGCCCTGATAGACGGTTTTTCGCCCTTTGACGTTGGAGTCCAC GTTCTTTAATAGTGGACTCTTGTTCCAAACTGGAACAACACTCAACCCTATCTCGGTCTATTCTT TTGATTTATAAGGGATTTTGCCGATTTCGGCCTATTGGTTAAAAAATGAGCTGATTTAACAAAAA TTTAACGCGAATTTTAACAAAATATTAACGCTTACAATTTCGCCTGTGTACCTTCTGAGGCGGAA AGAACCAGCTGTGGAATGTGTCAGTTAGGGTGTGGAAAGTCCCCAGGCTCCCCAGCAGCAGA AGTATGCAAAGCATGCATCTCAATTAGTCAGCAACCAGGTGTGGAAAGTCCCCAGGCTCCCCAGC AGGCAGAAGTATGCAAAGCATCCTCAATTAGTCAGCAACCATAGTCCCGCCCCTAACTCCGC

ATTTATGCAGAGGCCGAGGCCGCCTCGGCCTCTGAGCTATTCCAGAAGTAGTGAGGAGGCTTTTT TGGAGGCCTAGGCTTTTGCAAAAAGCTTGATTCTTCTGACACAACAGTCTCGAACTTAAGGCTAG AGCCACCATGATTGAACAAGATGGATTGCACGCAGGTTCTCCGGCCGCTTGGGTGGAGAGGCTAT TCGGCTATGACTGGGCACAACAGACAATCGGCTGCTCTGATGCCGCCGTGTTCCGGCTGTCAGCG GGCAGCGGGCTATCGTGGCCACGACGGGCGTTCCTTGCGCAGCTGTGCTCGACGTTGTCA CTGAAGCGGGAAGGGACTGCTGTTATTGGGCGAAGTGCCGGGGCAGGATCTCCTGTCATCTCAC CTTGCTCCTGCCGAGAAAGTATCCATCATGGCTGATGCAATGCGGCGGCTGCATACGCTTGATCC CCGGTCTTGTCGATCAGGATGATCTGGACGAAGAGCATCAGGGGCTCGCGCCAGCCGAACTGTTC GCCAGGCTCAAGGCGCGATGCCCGACGGCGAGGATCTCGTCGTGACCCATGGCGATGCCTGCTT GCCGAATATCATGGTGGAAAATGGCCGCTTTTCTGGATTCATCGACTGTGGCCGGCTGGGTGTGG CGGACCGCTATCAGGACATAGCGTTGGCTACCCGTGATATTGCTGAAGAGCTTGGCGGCGAATGG GCTGACCGCTTCCTCGTGCTTTACGGTATCGCCGCTCCCGATTCGCAGCGCATCGCCTTCTATCG CCTGCCATCACGATGGCCGCAATAAAATATCTTTATTTTCATTACATCTGTGTGTTGTTTTTTG TGTGAAGATCCGCGTATGGTGCACTCTCAGTACAATCTGCTCTGATGCCGCATAGTTAAGCCAGC CCCGACACCCGCCAACACCCGCTGACGCCCTGACGGGCTTGTCTGCTCCCGGCATCCGCTTAC AGACAAGCTGTGACCGTCTCCGGGAGCTGCATGTGTCAGAGGTTTTCACCGTCATCACCGAAACG CGCGAGACGAAAGGGCCTCGTGATACGCCTATTTTTATAGGTTAATGTCATGATAATAATGGTTT CTTAGACGTCAGGTGGCACTTTTCGGGGAAATGTGCGCGGAACCCCTATTTGTTTATTTTTCTAA ATACATTCAAATATGTATCCGCTCATGAGACAATAACCCTGATAAATGCTTCAATAATATTGAAA AAGGAAGAGTATGAGTATTCAACATTTCCGTGTCGCCCTTATTCCCTTTTTTGCGGCATTTTTGCC TTCCTGTTTTTGCTCACCCAGAAACGCTGGTGAAAGTAAAAGATGCTGAAGATCAGTTGGGTGCA CGAGTGGGTTACATCGAACTGGATCTCAACAGCGGTAAGATCCTTGAGAGTTTTCGCCCCGAAGA ACGTTTTCCAATGATGAGCACTTTTAAAGTTCTGCTATGTGGCGCGGTATTATCCCGTATTGACG CCGGGCAAGAGCAACTCGGTCGCCGCATACACTATTCTCAGAATGACTTGGTTGAGTACTCACCA GTCACAGAAAAGCATCTTACGGATGGCATGACAGTAAGAGAATTATGCAGTGCTGCCATAACCAT GAGTGATAACACTGCGGCCAACTTACTTCTGACAACGATCGGAGGACCGAAGGAGCTAACCGCTT ATACCAAACGACGAGCGTGACACCACGATGCCTGTAGCAATGGCAACAACGTTGCGCAAACTATT TTGCAGGACCACTTCTGCGCTCGGCCCTTCCGGCTGGTTTATTGCTGATAAATCTGGAGCC GGTGAGCGTGGGTCTCGCGGTATCATTGCAGCACTGGGGCCAGATGGTAAGCCCTCCCGTATCGT AGTTATCTACACGACGGGGAGTCAGGCAACTATGGATGAACGAAATAGACAGATCGCTGAGATAG GTGCCTCACTGATTAAGCATTGGTAACTGTCAGACCAAGTTTACTCATATATACTTTAGATTGAT TTAAAACTTCATTTTTAATTTAAAAGGATCTAGGTGAAGATCCTTTTTGATAATCTCATGACCAA AATCCCTTAACGTGAGTTTTCGTTCCACTGAGCGTCAGACCCCGTAGAAAAGATCAAAGGATCTT GTGGTTTGTTTGCCGGATCAAGAGCTACCAACTCTTTTTCCGAAGGTAACTGGCTTCAGCAGAGC GCAGATACCAAATACTGTCCTTCTAGTGTAGCCGTAGTTAGGCCACCACTTCAAGAACTCTGTAG TGTCTTACCGGGTTGGACTCAAGACGATAGTTACCGGATAAGGCGCAGCGGTCGGGCTGAACGGG GGGTTCGTGCACACAGCCCAGCTTGGAGCGAACGACCTACACCGAACTGAGATACCTACAGCGTG AGCTATGAGAAAGCGCCACGCTTCCCGAAGGGAGAAAGGCGGACAGGTATCCGGTAAGCGGCAGG GTCGGAACAGGAGCGCACGAGGGAGCTTCCAGGGGGAAACGCCTGGTATCTTTATAGTCCTGT GGAAAAACGCCAGCAACGCGGCCTTTTTACGGTTCCTGGCCTTTTGCTGGCCTTTTGCTCACATG GCTCGACAGATCT

TCAATATTGGCCATTAGCCATATTATTCATTGGTTATATAGCATAAATCAATATTGGCTATTGGC CATTGCATACGTTGTATCTATATCATAATATGTACATTTATATTGGCTCATGTCCAATATGACCG CCATGTTGGCATTGATTATTGACTAGTTATTAATAGTAATCAATTACGGGGTCATTAGTTCATAG CCCATATATGGAGTTCCGCGTTACATAACTTACGGTAAATGGCCCGCCTGGCTGACCGCCCAACG ACCCCCGCCCATTGACGTCAATAATGACGTATGTTCCCATAGTAACGCCAATAGGGACTTTCCAT TGACGTCAATGGGTGGAGTATTTACGGTAAACTGCCCACTTGGCAGTACATCAAGTGTATCATAT GCCAAGTCCGCCCCTATTGACGTCAATGACGGTAAATGGCCCGCCTGGCATTATGCCCAGTACA TGACCTTACGGGACTTTCCTACTTGGCAGTACATCTACGTATTAGTCATCGCTATTACCATGGTG ATGCGGTTTTGGCAGTACACCAATGGGCGTGGATAGCGGTTTGACTCACGGGGATTTCCAAGTCT CCACCCCATTGACGTCAATGGGAGTTTGTTTTGGCACCAAAATCAACGGGACTTTCCAAAATGTC GTAACAACTGCGATCGCCCGCCCGTTGACGCAAATGGGCGGTAGGCGTGTACGGTGGGAGGTCT ATATAAGCAGAGCTCGTTTAGTGAACCGTCAGATCACTAGAAGCTTTATTGCGGTAGTTTATCAC AGTTAAATTGCTAACGCAGTCAGTGCTTCTGACACACAGTCTCGAACTTAAGCTGCAGTGACTC TCTTAAGGTAGCCTTGCAGAAGTTGGTCGTGAGGCACTGGGCAGGTAAGTATCAAGGTTACAAGA GGCACCTATTGGTCTTACTGACATCCACTTTGCCTTTCTCTCCACAGGTGTCCACTCCCAGTTCA CTCCTGAAAGATGGAGGCGTCGCTGCCGGCCCAGGCCGCGAGACGGAGGAGGTGGGTCTTTTCG TCGAAAAATACCTCCGGTCCGATGTCGCGCCGGCGGAAATTGTCGCGCTCATGCGCAACCTCAAC AGCCTGATGGGACGCACGCGTTTATTTACCTGGCGTTGCTGGAGGCCTGTCTCCGCGTTCCCAT GGCCACCGCAGCAGCGCCATATTTCGGCGGATCTATGACCACTACGCCACGGGCGTCATCCCCA CGATCAACGTCACCGGAGAGCTGGAGCTCGTGGCCCTGCCCCCACCCTGAACGTAACCCCCGTC TGGGAGCTGTTGTGCCTGTGCAGCACCATGGCCGCGCCTGCATTGGGACTCGGCGGCCGGGGG ATCTGGGAGGACCTTCGGCCCCGATGACGTGCTGGACCTACTGACCCCCCACTACGACCGCTACA TGCAGCTGGTGTTCGAACTGGGCCACTGTAACGTAACCGACGGACTTCTGCTCTCGGAGGAAGCC GTCAAGCGCGTCGCCGACGCCCTAAGCGGCTGTCCCCCGCGCGGGTCCGTTAGCGAGACGGACCA CGCGGTGGCGCTGTTCAAGATAATCTGGGGCGAACTGTTTGGCGTGCAGATGGCCAAAAGCACGC AGACGTTTCCCGGGGCGGGGGCGTTAAAAACCTCACCAAACAGACAATCGTGGGGTTGTTGGAC GCCCACCACATCGACCACAGCGCCTGCCGGACCCACAGGCAGCTGTACGCCCTGCTTATGGCCCA CAAGCGGGAGTTTGCGGGCGCGCGTTCAAGCTACGCGTGCCCGCGTGGGGGCCGCTGTTTGCGCA CGCACTCATCCAGCGCCAACCCCAACGCTGACATCATCCTGGAGGCGGCGCTGTCGGAGCTCCCC ACCGAGGCCTGGCCCATGATGCAGGGGGGGGGTGAACTTTAGCACCCTACCAAAAAAGAAGAAAAA GGTAGATCGGACACTGGTGACCTTCAAGGATGTATTTGTGGACTTCACCAGGGAGGAGTGGAAGC TGCTGGACACTGCTCAGCAGATCGTGTACAGAAATGTGATGCTGGAGAACTATAAGAACCTGGTT TCCTTGGGTTATTGATGAGATATCATCTAGAGCGGCCGCAGGTACCTGAATAACTAAGGCCGCTT CCCTTTAGTGAGGGTTAATGCTTCGAGCAGACATGATAAGATACATTGATGAGTTTGGACAAACC ACAACTAGAATGCAGTGAAAAAAATGCTTTATTTGTGAAATTTGTGATGCTATTGCTTTATTTGT AACCATTATAAGCTGCAATAAACAAGTTAACAACAACAATTGCATTCATGTTTCAGGTTC AGGGGGAGATGTGGGAGGTTTTTTAAAGCAAGTAAAACCTCTACAAATGTGGTAAAATCCGATAA TGTGGTGGTTACGCGCACGTGACCGCTACACTTGCCAGCGCCCTAGCGCCCCGCTCCTTTCGCTTT CTTCCCTTCCTTTCTCGCCACGTTCGCCGGCTTTCCCCGTCAAGCTCTAAATCGGGGGCTCCCTT TAGGGTTCCGATTTAGTGCTTTACGGCACCTCGACCCCAAAAAACTTGATTAGGGTGATGGTTCA CGTAGTGGGCCATCGCCCTGATAGACGGTTTTTCGCCCTTTGACGTTGGAGTCCACGTTCTTTAA TAGTGGACTCTTGTTCCAAACTGGAACACACTCAACCCTATCTCGGTCTATTCTTTTGATTTAT AAGGGATTTTGCCGATTTCGGCCTATTGGTTAAAAAATGAGCTGATTTAACAAAAATTTAACGCG AATTTTAACAAAATATTAACGCTTACAATTTCGCCTGTGTACCTTCTGAGGCGGAAAGAACCAGC TATGCAAAGCATGCATCTCAATTAGTCAGCAACCATAGTCCCGCCCCTAACTCCGCCCATCCCGC

FIGURE 15A

GAGGCCGAGGCCTCTGGGCCTCTGAGCTATTCCAGAAGTAGTGAGGAGGCTTTTTTTGGAGGCCT AGGCTTTTGCAAAAAGCTTGATTCTTCTGACACAACAGTCTCGAACTTAAGGCTAGAGCCACCAT GATTGAACAAGATGGATTGCACGCAGGTTCTCCGGCCGCTTGGGTGGAGAGGCTATTCGGCTATG ACTGGGCACAACAGACAATCGGCTGCTCTGATGCCGCCGTGTTCCGGCTGTCAGCGCAGGGGCGC GCTATCGTGGCTGGCCACGACGGCGTTCCTTGCGCAGCTGTGCTCGACGTTGTCACTGAAGCGG GAAGGGACTGCTGTTTTGGGCGAAGTGCCGGGGCAGGATCTCCTGTCATCTCACCTTGCTCCT GCCGAGAAAGTATCCATCATGGCTGATGCAATGCGGCGGCTGCATACGCTTGATCCGGCTACCTG CCCATTCGACCAAGCGAAACATCGCATCGAGCGAGCACGTACTCGGATGGAAGCCGGTCTTG TCGATCAGGATGATCTGGACGAAGAGCATCAGGGGCTCGCGCCAGCCGAACTGTTCGCCAGGCTC AAGGCGCGCATGCCCGACGGCGAGGATCTCGTCGTGACCCATGGCGATGCCTGCTTGCCGAATAT CATGGTGGAAAATGGCCGCTTTTCTGGATTCATCGACTGTGGCCGGCTGGGTGTGGCGGACCGCT ATCAGGACATAGCGTTGGCTACCCGTGATATTGCTGAAGAGCTTGGCGGCGAATGGGCTGACCGC TTCCTCGTGCTTTACGGTATCGCCGCTCCCGATTCGCAGCGCATCGCCTTCTATCGCCTTCTTGA ACGATGGCCGCAATAAAATATCTTTATTTTCATTACATCTGTGTGTTGGTTTTTTTGTGTGAAGAT CGCCAACACCCGCTGACGCCCTGACGGGCTTGTCTGCTCCCGGCATCCGCTTACAGACAAGCT GTGACCGTCTCCGGGAGCTGCATGTGTCAGAGGTTTTCACCGTCATCACCGAAACGCGCGAGACG AAAGGGCCTCGTGATACGCCTATTTTTATAGGTTAATGTCATGATAATAATGGTTTCTTAGACGT CAGGTGGCACTTTTCGGGGAAATGTGCGCGGAACCCCTATTTGTTTATTTTTCTAAATACATTCA AATATGTATCCGCTCATGAGACAATAACCCTGATAAATGCTTCAATAATATTGAAAAAGGAAGAG TATGAGTATTCAACATTTCCGTGTCGCCCTTATTCCCTTTTTTGCGCCATTTTTGCCTTCCTGTTT TTGCTCACCCAGAAACGCTGGTGAAAGTAAAAGATGCTGAAGATCAGTTGGGTGCACGAGTGGGT TACATCGAACTGGATCTCAACAGCGGTAAGATCCTTGAGAGTTTTCGCCCCGAAGAACGTTTTCC AATGATGAGCACTTTTAAAGTTCTGCTATGTGGCGCGGTATTATCCCGTATTGACGCCGGGCAAG AGCAACTCGGTCGCCGCATACACTATTCTCAGAATGACTTGGTTGAGTACTCACCAGTCACAGAA AAGCATCTTACGGATGGCATGACAGTAAGAGAATTATGCAGTGCTGCCATAACCATGAGTGATAA CACTGCGGCCAACTTACTTCTGACAACGATCGGAGGACCGAAGGAGCTAACCGCTTTTTTGCACA GACGAGCGTGACACCACGATGCCTGTAGCAATGGCAACAACGTTGCGCAAACTATTAACTGGCGA CACTTCTGCGCTCGGCCTTCCGGCTGGCTGGTTTATTGCTGATAAATCTGGAGCCGGTGAGCGT GGGTCTCGCGGTATCATTGCAGCACTGGGGCCAGATGGTAAGCCCTCCCGTATCGTAGTTATCTA CACGACGGGGAGTCAGGCAACTATGGATGAACGAAATAGACAGATCGCTGAGATAGGTGCCTCAC CATTTTTAATTTAAAAGGATCTAGGTGAAGATCCTTTTTGATAATCTCATGACCAAAATCCCTTA ACGTGAGTTTTCGTTCCACTGAGCGTCAGACCCCGTAGAAAAGATCAAAGGATCTTCTTGAGATC CTTTTTTTCTGCGCGTAATCTGCTGCTTGCAAACAAAAAACCACCGCTACCAGCGGTGGTTTGT TTGCCGGATCAAGAGCTACCAACTCTTTTTCCGAAGGTAACTGGCTTCAGCAGAGCGCAGATACC AAATACTGTCCTTCTAGTGTAGCCGTAGTTAGGCCACCACTTCAAGAACTCTGTAGCACCGCCTA CATACCTCGCTCTGCTAATCCTGTTACCAGTGGCTGCCAGTGGCGATAAGTCGTGTCTTACC GGGTTGGACTCAAGACGATAGTTACCGGATAAGGCGCAGCGGTCGGGCTGAACGGGGGGTTCGTG CACACAGCCCAGCTTGGAGCGAACGACCTACACCGAACTGAGATACCTACAGCGTGAGCTATGAG AAAGCGCCACGCTTCCCGAAGGGAGAAAGGCGGACAGGTATCCGGTAAGCGGCAGGGTCGGAACA GGAGAGCGCACGAGGGAGCTTCCAGGGGGAAACGCCTGGTATCTTTATAGTCCTGTCGGGTTTCG CCAGCAACGCGGCCTTTTTACGGTTCCTGGCCTTTTGCTGGCCTTTTGCTCACATGGCTCGACAG ATCT

FIGURE 15B